

**WHAT IS CLAIMED IS:**

1. An isolated L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 2.
2. The polypeptide of claim 1, wherein the KIVA sequence is in an extracellular domain.
3. The polypeptide of claim 1, wherein the polypeptide is human.
4. The polypeptide of claim 1, wherein the polypeptide does not include the amino acid sequence of SEQ ID NO: 10.
5. The polypeptide of claim 1, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 4.
6. The polypeptide of claim 1, wherein the polypeptide consists of the amino acid sequence of SEQ ID NO: 4.
7. An isolated L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide, wherein the polypeptide comprises an amino acid sequence at least 85% homologous to SEQ ID NO: 6, and wherein the polypeptide comprises one or more of the following features:
  - (a) a deletion of amino acids 1291-1305 of SEQ ID NO: 6;
  - (b) an insertion of SEQ ID NO: 2; or
  - (c) a deletion of amino acids 1804-1812 of SEQ ID NO: 6.
8. The polypeptide of claim 7, wherein the polypeptide comprises the insertion of SEQ ID NO: 2, and wherein the insertion is in an extracellular domain.
9. The polypeptide of claim 8, wherein the insertion is between the third and fourth transmembrane segments of a repeat domain.
10. The polypeptide of claim 9, wherein the insertion is between the third and fourth transmembrane segments of the fourth repeat domain.
11. The polypeptide of claim 10, wherein the insertion is after amino acid 1290 of SEQ ID NO: 6.
12. The polypeptide of claim 10, wherein the insertion is at amino acid 1290 of SEQ ID NO: 6.

13. The polypeptide of claim 7, wherein the polypeptide has any two of the features (a), (b), or (c).
14. The polypeptide of claim 7, wherein the polypeptide has all three of the features (a), (b), or (c).
15. An isolated polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 4, wherein the polypeptide includes at least one of amino acids 1281-1284 and/or amino acids 1792 and 1793.
16. The polypeptide of claim 2, wherein a portion of the extracellular domain, but not SEQ ID NO: 2, is replaced by an extracellular domain from another calcium channel  $\alpha_1$  subunit.
17. An isolated L-type calcium  $\alpha_{1D+KIVA}$  subunit nucleic acid molecule that encodes the polypeptide of any of claims 1-16.
18. The nucleic acid molecule of claim 17, wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 3.
19. The nucleic acid molecule of claim 18, wherein the nucleic acid molecule consists of the nucleotide sequence of SEQ ID NO: 3.
20. The nucleic acid molecule of claim 17, wherein the nucleic acid is an allele of the nucleic acid sequence of SEQ ID NO: 3.
21. A fragment of the L-type calcium  $\alpha_{1D+KIVA}$  subunit nucleic acid molecule of claim 17, wherein the fragment encodes SEQ ID NO: 2.
22. An expression vector comprising the L-type calcium  $\alpha_{1D+KIVA}$  subunit nucleic acid molecule of claim 17 operably linked to a promoter.
23. A host cell comprising the nucleic acid of claim 17.
24. An agent which preferentially binds to the L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide of claim 1.
25. An agent which binds selectively to the L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide of claim 5 and not to an L-type calcium channel  $\alpha_{1D}$  subunit polypeptide comprising the sequence of SEQ ID NO: 5.
26. The agent of claim 24, wherein the agent is a small molecule, a nucleic acid, or a protein.

27. The agent of claim 26, wherein the agent modulates (e.g., inhibits or enhances) calcium channel activity of the L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide.
28. The agent of claim 26, wherein the agent is an antibody or antigen-binding fragment thereof.
29. The agent of claim 28, wherein the antibody is a polyclonal antibody or monoclonal antibody.
30. A pharmaceutical composition comprising the agent of claim 27 and a pharmaceutically acceptable carrier.
31. A method for modulating an L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide activity in a cell, the method comprising:
  - providing an L-type calcium channel comprising an  $\alpha_{1D+KIVA}$  subunit polypeptide, wherein the  $\alpha_{1D+KIVA}$  subunit polypeptide is according to any of claims 1-16;
  - contacting the channel with an amount of an L-type calcium channel  $\alpha_{1D+KIVA}$  subunit modulator effective to modulate an activity of the  $\alpha_{1D+KIVA}$  subunit polypeptide.
32. The method of claim 31, wherein the modulator is a small molecule, a nucleic acid, or a protein.
33. A method for identifying an agent that modulates the activity of an L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide, the method comprising:
  - providing a first calcium channel comprising an  $\alpha_{1D+KIVA}$  subunit polypeptide, wherein the  $\alpha_{1D+KIVA}$  subunit polypeptide is according to any of claims 1-16;
  - contacting the channel with a test compound; and
  - evaluating an activity of the calcium channel, wherein a change in activity relative to a reference value is an indication that the compound is an agent that modulates the channel.
34. The method of claim 33, wherein the test compound is a small molecule, a peptide, or a nucleic acid.
35. The method of claim 33, wherein the calcium channel is contained within a biological sample.

36. The method of claim 35, wherein the sample comprises a cell membrane.
37. The method of claim 36, wherein the sample comprises a cell.
38. The method of claim 37, wherein the cell is a eukaryotic cell.
39. The method of claim 38, wherein the cell is *Xenopus* oocyte.
40. The method of claim 38, wherein the cell is a mammalian cell.
41. The method of claim 33, wherein the activity comprises regulation of calcium concentration.
42. The method of claim 41, wherein the evaluating comprises detecting calcium flux.
43. The method of claim 42, wherein the contacting occurs under conditions which, in the absence of the test compound, cause a first amount of calcium flux.
44. The method of claim 42, wherein the evaluating comprises using a calcium flux assay.
45. The method of claim 43, wherein the assay uses patch clamp electrophysiology.
46. The method of claim 43, wherein the assay uses two electrode voltage clamp electrophysiology.
47. The method of claim 43, wherein the assay is a fluorescence assay.
48. The method of claim 33, further comprising the steps of:
  - providing a second calcium channel comprising an  $\alpha_{1D}$  subunit polypeptide, wherein the  $\alpha_{1D}$  subunit polypeptide is other than an  $\alpha_{1D+KIVA}$  subunit polypeptide according to claims 1-16;
  - contacting the second channel with the test compound;
  - evaluating the activity of the second calcium channel.
49. The method of claim 48, further comprising comparing the activity of the first calcium channel in the presence of the test compound to the activity of the second calcium channel in the presence of the test compound.
50. The method of claim 33, wherein a plurality of calcium channels are provided.
51. The method of claim 33, wherein the  $\alpha_{1D+KIVA}$  subunit polypeptide comprises the amino acid sequence of SEQ ID NO: 4.
52. A method for identifying an agent which selectively binds an L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide isoform, the method comprising:
  - providing a first  $\alpha_{1D+KIVA}$  subunit polypeptide isoform according to any of

claims 1-16;

contacting the first polypeptide with a test compound;

assaying binding of the test compound to the first polypeptide;

providing a second  $\alpha_{1D}$  subunit polypeptide, wherein the  $\alpha_{1D}$  subunit polypeptide is other than an  $\alpha_{1D+KIVA}$  subunit polypeptide according to claims 1-16

contacting the second polypeptide with the test compound;

assaying binding of the test compound to the second polypeptide, wherein a compound which binds the first polypeptide and does not substantially bind the second polypeptide is an indication that the compound is an agent which selectively binds an L-type calcium channel  $\alpha_{1D+KIVA}$  subunit polypeptide isoform.

53. A method for identifying an agent useful in the treatment of a disorder related to calcium current, the method comprising:
- providing a calcium channel comprising an  $\alpha_{1D+KIVA}$  subunit polypeptide according to any of claims 1-16;
  - contacting the channel with a test compound; and
  - evaluating an activity of the channel, wherein a change in activity relative to a reference value is an indication that the test compound is an agent useful in a disorder related to calcium current.
54. The method of claim 53, wherein the disorder is a heart disorder,
55. The method of claim 53, further comprising administering the compound in vivo (e.g., using an animal model).
56. The method of claim 53, further comprising modifying the compound for use in vivo.
57. A method for treating a subject having a disorder related to calcium channel current, the method comprising:
- administering to a subject in need of such treatment a pharmacological agent which is selective for a calcium channel comprising an  $\alpha_{1D+KIVA}$  subunit.
58. The method of claim 57, wherein the disorder is a heart disorder.